

Arteriovenous malformation: A review of four cases*

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INTRODUCTION

Uterine arteriovenous malformation (AVM) is a rare disorder characterized by multiple abnormal communications between arteries and veins. Although its true incidence is unknown, it has been thought to be more common than reported, with more cases of traumatic AVMs being increasingly diagnosed⁴.

Due to its rarity, a high index of suspicion and timely and accurate diagnosis is especially imperative, as instrumentation often used for other sources of uterine bleeding may lead to massive hemorrhage.

This report presents 4 cases of arteriovenous malformation seen and diagnosed at our institution in 2006, 2012, 2015 and most recently, January 2016.

This report aims to compare the 4 cases, the arrival at a diagnosis and subsequent management, thereby presenting a more comprehensive clinical examination of this rare condition. Because of its nature and highly variable presentation, it is often overlooked when searching for a differential diagnosis. This study aims to present Uterine AVM as a possible consideration in all women of reproductive age presenting with unexplained, intermittent, profuse vaginal bleeding.

CASE REPORT

CASE 1

J.F. is a 23-year-old G1P0 (0010), admitted on January 2016 due to heavy menstrual bleeding.

Four months prior to admission, pregnancy test done was positive. TVS done showed no cardiac activity. Patient also noted vaginal bleeding consuming 1-2 regular pads. Repeat ultrasound done after 1 week, still showed no cardiac activity. Vaginal bleeding spontaneously resolved and patient advised to await signs of spontaneous passage of products of conception.

Three months prior to admission, with note of recurrence of vaginal bleeding, accompanied by passage of meaty tissues and tolerable crampy, hypogastric pain. Transvaginal ultrasound done by AMD showed retained

products of conception. She was then scheduled for, and underwent completion curettage, with no complications noted. With temporary resolution of vaginal bleeding until 12 days post curettage, when there was recurrence of intermittent vaginal spotting staining 2-3 pantyliners. Patient followed up with AMD, where TVS with Doppler done showed a heterogenous structure within the fundal myometrium measuring 1.85 x 1.61 x 1.11cm with serpiginous vascular flow on color mapping. B-hcg requested was elevated at 75.74 mg/dL. Impression was to consider arteriovenous malformation. No further management done and advised to observe bleeding.

Interval history shows spontaneous resolution of bleeding until 1 week prior to consult (61 days post curettage), when there was recurrence of heavy menstrual bleeding, staining 1 pantyliner to consuming 6 regular pads, fully soaked, with blood clots, and soaking bedsheets. Patient followed up with AMD where pelvic CT angiography requested showed uterine arteriovenous malformation with arterial supply from the bilateral uterine arteries. Repeat Doppler ultrasound showed an irregular heterogenous structure with multiple cystic areas occupying the upper anterior myometrium and extending to the mid portion measuring 2.33 x 2.15 x 1.53cm. Color Doppler showed the mass to be hypervascular with massive turbulent flow (Figure 1). She was started on Tranexamic acid and subsequently admitted for embolization of bilateral uterine arteries.

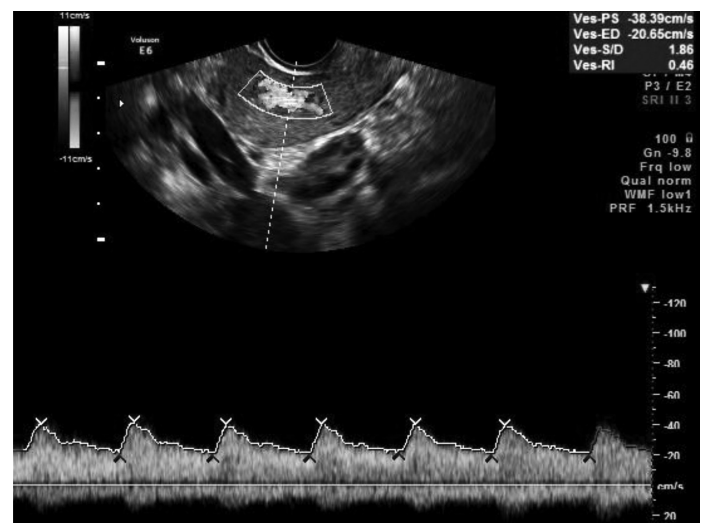


Figure 1. (CASE 1) Mosaic/serpiginous pattern characteristic of AVM on Doppler ultrasound

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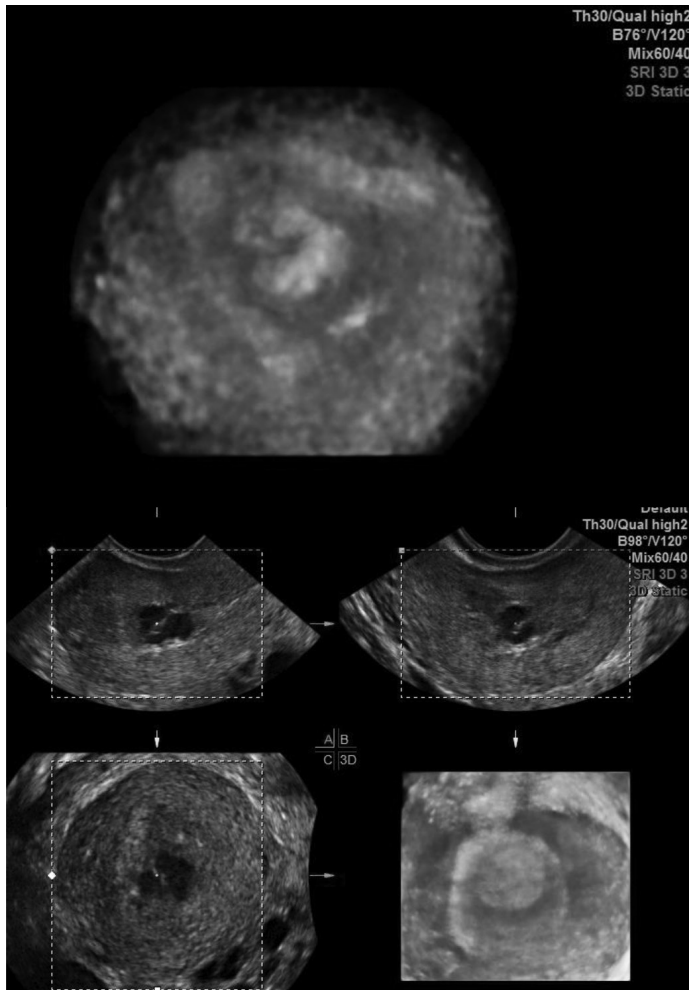


Figure 2. (CASE 1) endometrial mass representing nidus of vessels, as visualized on 3D ultrasound

Embolization of bilateral uterine arteries was done using Polyvinyl Alcohol Particles, with intra-operative findings of AV Malformation in the right upper uterine segment with blood arising from the right uterine artery and an intra-nidal aneurysm. Although left internal angiogram showed no definite supply to the arteriovenous malformation, embolization was also done to prevent recurrence from collateralization. Post embolization of Right and Left Internal Iliac arteries showed no definite supply to the arteriovenous malformation (Figure 3). Patient tolerated the procedure well and was discharged stable on the 8th hospital day.

Repeat transvaginal ultrasound was done post embolization showed a homogenous structure at the endometrial cavity, probably remnants of occluded vessels, with no flow visualized on color mapping.

Case 2

K.M. is a 38-year-old G2P2 (1102) s/p Diagnostic D&C x 2 (1st – decidual tissues, 2nd – endometrial polyp) who came in due to heavy postpartum vaginal bleeding.

Her first pregnancy was uncomplicated and delivered

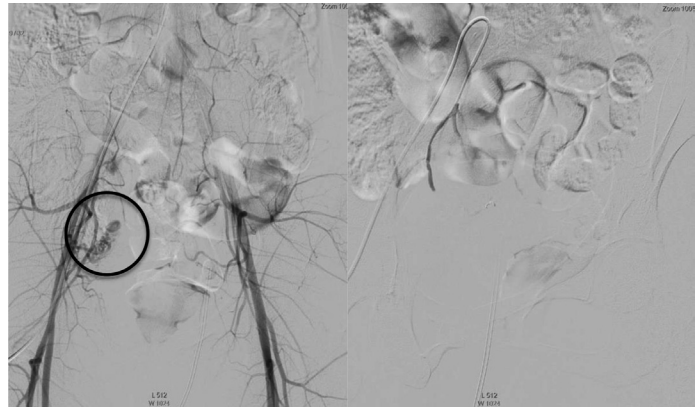


Figure 3. (CASE 1) AVM originating from the Right Internal Iliac Artery (pre embolization); No AVM appreciated arising from the Left internal Iliac artery; compared to post embolization imaging

via primary cesarean section for non reassuring fetal status. Past Medical and Gynecologic history were uncomplicated and non-contributory.

Two months prior to admission, on approximately day 13 postpartum, patient noted increase in vaginal bleeding consuming 5 maternity pads fully soaked, with blood clots. She was then admitted at our institution where Transvaginal ultrasound showed an enlarged anteverted uterus with thickened endometrium at 2.76cm; dilated endocervical canal with blood clots (volume of 8.44mL); fluid collection within the anterior lower uterine segment or cesarean section scar with intact serosal surface; consider blood clots vs retained placental tissue/membranes within the fundal cavity and normal ovaries.

Impression was retained placental secundines for which she then underwent dilatation and curettage. The histopathologic finding was predominantly blood clots with fibrinous tissues, showing acute on chronic inflammation and decidual tissues. Blood transfusion of 4 units of blood given and discharged stable; with no active bleeding noted.

One month prior to admission, on approximately day 32 postpartum, patient had recurrence of heavy menstrual bleeding described as consuming 1 pantyliner per day, fully soaked, with blood clots. She then consulted at the ER of another institution where CBC done showed a hemoglobin of 6.8mg/dL. She was admitted, transfused with 3 units pRBC, and again underwent dilatation and curettage, revealing an endometrial polyp, proliferative endometrium and fragments of benign ectocervical tissue.

Fourteen days prior to admission, on approximately day 43 postpartum, repeat ultrasound done by an OB sonologist, showed an intact anterior lower uterine segment measuring 0.79cm. An anechogenic ovoid structure was noted within the uterus at the right corneal area measuring 1.57 x 1.01 x 0.98 cm. The intrauterine mass noted may be a placental tissue or a clotted blood.

Twelve days prior to admission, on day 45 postpartum, patient had recurrence of heavy menstrual bleeding, as described, now associated with hypotension, with BP at 80/60 and PR 126. Transvaginal ultrasound done on admission showed: normal sized midpositioned uterus measuring 5.08 x 5.43 x 4.91 cm with no focal mass seen. Endometrial thickness at 1cm with note of fluid motion within. IMPRESSION: Normal sized midpositioned uterus with intact and hyperechoic endometrium.

CBC done showed a hemoglobin of 6.9mg/dL. Admitted and transfused with 3 units Fresh Whole Blood and 1 unit pRBC. Repeat CBC post transfusion revealed a hemoglobin of 10.6mg/dL.

Patient was sent home with Progesterone only contraceptive pill and Ferrous Sulfate. Bleeding resolved and patient was asymptomatic until few hours prior to admission, patient noted recurrence of vaginal bleeding fully soaking 1 regular pad and 1 adult diaper, with blood clots. Patient was admitted at our institution, started on Tranexamic Acid 500mg IV and Micropill 1 cap TID for hemostasis and advised to continue ferrous sulfate BID. Transfused with 1 unit pRBC for correction of anemia. During admission, a transvaginal ultrasound was repeated (on day 57 postpartum) and revealed normal sized retroverted uterus measuring 5.29 x 5 x 5.54 cm. No focal mass seen. Cervix measures 2.72 x 3.42 x 4.03 cm. The endocervical canal is heterogenous and slightly dilated to 0.32 cm. Color flow shows increased stromal vascularity with complex serpentine vessel pattern and distinct venous and arterial waveforms. Endometrium measures 0.46cm. Intact subendometrial halo. Within the anterior lower uterine segment are irregular hypoechoic areas surrounded by hyperechoic border measuring 1.94 x 0.90cm. Color Doppler shows hypervascularity juxtaposed with orange and blue mosaic pattern with high velocity waveforms (Figure 4). Superior and lateral to the uterine corpus is a thin walled (0.18cm) cystic structure measuring 7.67 x 4.20 x 6.40cm (previously 6.91 x 6.55 x 3.73cm) with low level echogenicity. Borders are vague on TVS however supplemental TAS shows cyst to be well defined with echogenic borders. No flow on color mapping but adjacent to right uterine vessels.

Impression: normal sized retroverted uterus with thin and intact endometrium; normal ovaries; hypervascular cervix; lower uterine segment heterogeneity with color flow pattern suggestive of AVM; right pelvic cyst, consider encysted fluid vs hematoma or hematosalpinx.

She then underwent total abdominal hysterectomy with right salpingoophorectomy, with intraoperative findings of (Figure 5): a slightly enlarged uterus measuring 6.5 x 5.5 x 2.3 cm. Endometrial thickness of 0.4 cm, smooth, with note of a 1.5 x 1.5 cm fleshy mass in the fundal area. Anterior wall measures 1.5 cm while the posterior wall



Figure 4. (CASE 2) Color Mosaic pattern seen on Doppler sonography: hypervascularity juxtaposed with orange and blue mosaic pattern with high velocity waveforms

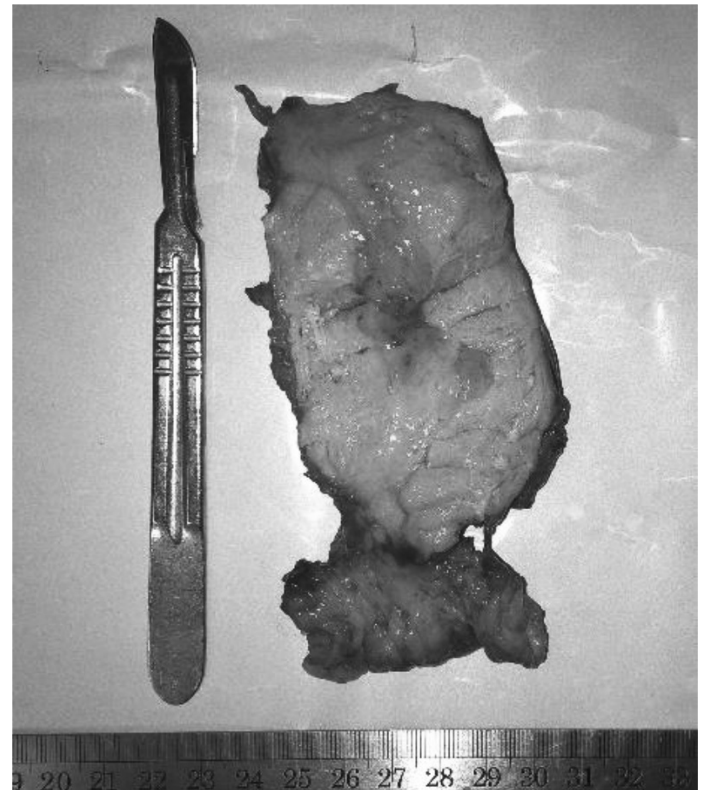


Figure 5. (CASE 2) gross appearance on TAHBSO

measures 1.6 cm, both with cystic spaces filled with blood. Right ovary converted to a multiloculated cystic structure measuring 5 x 5 x 2.5 cm, with chocolate like fluid on inadvertent rupture. Left fallopian tube and Left ovary were grossly normal in appearance.

Histopathology done showed chronic cervicitis with squamous metaplasia. Adenomyosis and Endometrial Polyp. Intramural thick and thin walled vascular channels present compatible with arteriovenous malformation.

Proliferative endometrium. Ovary, Right, Endometrial Cyst. Fallopian tube, right, No diagnostic abnormality recognized.

The rest of the hospital stay was unremarkable and she was discharged stable, with no complaints.

Case 3

J.A., a 24-year-old, G1P0 (0010), was admitted in July 2012 due to vaginal bleeding.

Three months prior to admission, patient underwent completion curettage for a miscarriage, which showed decidual tissues and endometritis on histopath.

Two weeks prior to admission, the patient noted vaginal bleeding consuming 4 to 5 pads per day with blood clots. Patient consulted with an obstetrician where a transvaginal ultrasound revealed an irregular, ill-defined complex mass with rich color flow occupying the lower one third of the uterus to the fundal area measuring 4.5 x 3.4 x 2.7 cm. Sonographic impression was "Cannot totally rule out an invasive mole versus an arteriovenous malformation". β -hCG done was normal at 1.46 mIU/mL. CBC revealed Hemoglobin of 8.4 mg/dL and she was transfused with 2 units of packed RBC. Repeat β -hCG done after 2 days was still normal limits at 1.46 g/dL. She was discharged stable with no vaginal bleeding, given ferrous fumarate and tranexamic acid, and advised transfer to a tertiary institution for further work-up.

One week prior to admission, patient had recurrence of vaginal bleeding now consuming 1 maternity pad, fully soaked with blood clots, for which she sought consult with AMD. On examination, patient had pale palpebral conjunctivae and nail beds, abdomen was soft and nontender, no palpable masses noted. Internal examination revealed a closed cervix and a slightly enlarged uterus. Patient underwent correction of anemia with transfusion of 2 units of packed RBC.

Repeat transvaginal ultrasound done revealed a myometrial multicystic hypervascular mass, to consider an arteriovenous malformation. CT angiography was performed which showed a conglomeration of tortuous vascular structures predominantly involving the anterior myometrium, supplied by a branch of the anterior division of the right internal iliac artery (Figure 5).

Patient subsequently underwent embolization of the right uterine artery using gel foam, with complete occlusion of the uterine artery on post injection and confirmatory angiography and discharged improved on the 2nd post-operative day.

One month after embolization, repeat ultrasound showed was a significant change in the appearance of the arteriovenous malformation on gray scale imaging, showing markedly reduced blood flow pattern on color doppler.

Two months after embolization, repeat ultrasound was again done, which showed a homogenous anterior myometrium, with no demonstrable arteriovenous malformation on gray scale imaging and flow only within the periphery of the myometrium on color doppler application. She was maintained on combined oral contraceptive pills with no recurrence of vaginal bleeding post operatively.

Case 4

A.C. is a 28-year-old G2P1 (1011), admitted in July 2006, who came in due to vaginal bleeding. First term pregnancy in 2004 was delivered via caesarean section for cephalopelvic disproportion.

3 months prior to admission, she underwent completion curettage for a miscarriage with an unremarkable hospital stay.

2 months prior to admission, patient noted vaginal bleeding consuming to 4 pads per day, occurring every 14 days and lasting for 5 days, accompanied by intermittent, non-radiating, crampy, hypogastric pain. Interval history showed persistence and worsening of the bleeding, however no consult was done.

One day prior to admission, the patient noted vaginal bleeding, with passage of blood clots, sought gynecologic consult and was admitted. Speculum examination showed minimal bleeding per os and moderate pooling of blood at the posterior fornix. On internal examination, the cervix was firm, short and closed, corpus not enlarged, with negative adnexae. The rest of the physical exam was normal and unremarkable. She was then advised subsequent admission. Assessment was Abnormal Uterine Bleeding, Rule Out Endometrial Pathology; Rule Out Gestational Trophoblastic Disease.

On admission, CBC showed hemoglobin of 11.2 mg/dL, and hematocrit of 0.34; Prothrombin and Partial Thromboplastin times were within normal limits. Qualitative serum β -hCG was negative.

Doppler ultrasound done demonstrated a complex vascular mass at the fundal portion with extension to the uterine cavity measuring 1.22 x 0.88 cm showing extensive color aliasing or inverting and apparent flow reversal. Endometrial stripe was 0.44 cm, hyperechoic, and the subendometrial halo appears intact except at the fundal portion where the complex vessels were noted. Doppler studies showed the endometrial mass to have a Resistance Index of 0.46 and a Pulsatility Index of 0.61. Impression was a Vascular Intrauterine Mass, to consider Arteriovenous Malformation, rule out Endometrial Pathology.

Initially patient was scheduled for pelvic laparotomy with conservative surgery. However, preoperatively, she had an episode of profuse vaginal bleeding with passage of

blood clots, after which she was noted to be hypotensive, with a blood pressure of palpatory 60, and tachycardic at 130 bpm. She was stabilized with intravenous fluids and colloids, transfused with 1 unit of fresh whole blood and underwent emergency exploration.

The specimen consisted of a creamy, sessile mass with irregular surface measuring approximately 3 cm showing multiple cystic spaces, blood vessels and purplish black cystic structure (Figure 6). Histopathology of the specimen revealed: Arteriovenous Malformation of the Endometrium; Simple Endometrial Hyperplasia without Atypia (Figure 7).



Figure 6. (CASE 4) A creamy, sessile mass with irregular surface measuring approximately 3 cm showing multiple cystic spaces, blood vessels and purplish black cystic structures was obtained

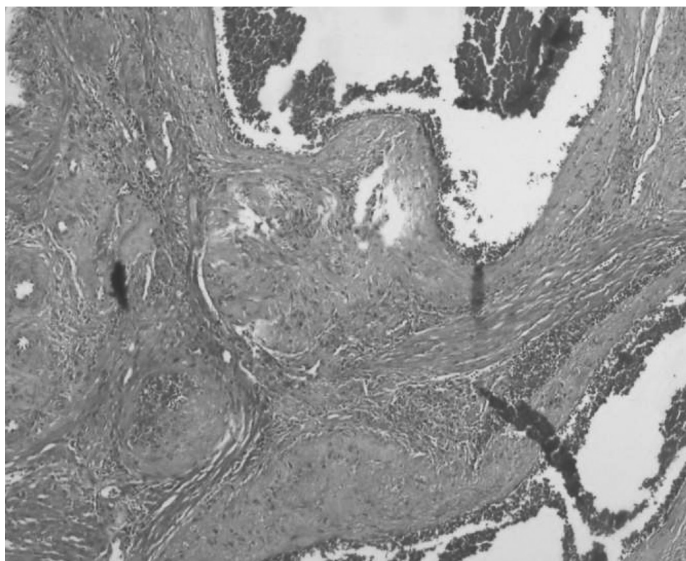


Figure 7. (CASE 4) Histopathology of the specimen showing lack of distinction between the arteries and veins, thickened intimal layer and absence of capillaries.



Figure 8. (CASE 4) CT angiogram showed conglomeration of tortuous vascular structures predominantly involving the anterior myometrium, supplied by branch of the anterior division of the right internal iliac artery And 3D reconstruction of the hypervascular mass showing conglomeration of tortuous vascular structures predominantly involving the anterior myometrium

She was given Depo-medroxyprogesterone acetate 150mg intramuscularly once a month for 3 doses with no recurrence of the abnormal uterine bleeding.

A year after the operation, a repeat transvaginal ultrasound was done which showed a slightly retroverted uterus, without any intramural or endometrial masses noted. Color doppler studies of uterine arcuate arteries were within normal limits (Resistance index: 0.65; Pulsatility index: 1.16 cm).

DISCUSSION

Uterine arteriovenous malformations are incredibly uncommon, with most literature available limited to case reports or case series; the first of which was written locally by Dr. JE Sy and published in 2003. The 27-year-old presented was a G4P3 (2112) who was diagnosed with AVM and subsequently underwent total abdominal hysterectomy².

The second published case was only reported in 2012 by Cacha and Moran, in which the 31-year-old patient, a G1P1 (1001), was diagnosed through CT angiography and underwent pelvic angiogram with transcatheter embolization of the left uterine artery³.

AVMs are a “proliferation of arterial and venous channels with fistula formation and an admixture of small capillary like channels”⁶, which may be classified as either congenital or acquired.

Congenital AVMs are due to the abnormal development of primitive vascular structures. Failure of vascular differentiation results to the multiple aberrant connections of arteries and veins⁴. Large flexiform structures formed in the mesenchyme differentiate into mature vessels, with the embryonic components regressing, or partially developing with the embryonic

vascular communications remaining. These AVMs are therefore considered focal areas of inadequate vascular development.

In contrast, acquired uterine AVMs are usually traumatic, following damage to uterine tissue. Known risk factors include previous curettage, cesarean section, gestational trophoblastic diseases, exposure to diethylstilbestrol, endometriosis, fibroids and endometrial or cervical cancers^{1,4}. It is suggested that acquired AVMs are merely an “unmasking” of a congenital type.

The lesions grow by recruiting collateral vascular channels. Due to the hormonal stimulation during menstrual cycles, disproportional growth may occur in women in their 20's, explaining the increased incidence of subclinical AVMs in this population. Pregnancy also appears to play a key role in the pathogenesis of AVMs, due to the connection of arterial and venous vessels within the myometrium during involution of the chorioplacental villi following cessation of pregnancy⁵.

All 4 cases presented with a history of a previous cesarean section or curettage. Given this background, and the absence of earlier confirmatory imaging or prior profuse bleeding, we may presume an acquired type of AVM for the latter 3 cases. Case 1, although also with a history of curettage, may be a congenital type given its supply arising from a large central artery, that was merely uncovered postoperatively.

The classical presentation of uterine AVM is often one of severe uterine bleeding with no obvious cause. The pattern of bleeding is usually intermittent and torrential (suggestive of arterial hemorrhage), and sometimes significant enough to require multiple blood transfusions¹. Repeated spontaneous miscarriages may also occur owing to vascular alterations at the site of embryonic implantation⁸.

The blood flow within AVMs is slow and under low pressure because of the many capillaries present. However histologically, in many cases, distinction between the arteries and veins become indistinct due to the increased venous intraluminal pressure and secondary intimal thickening¹. Congenital AVMs tend to have multiple feeding arteries, draining veins, and an intervening nidus, whereas acquired AVMs, which form between intramural arterial branches and the myometrial venous plexus, tend to possess single or bilateral feeding arteries, are not supplied by extrauterine arteries, and do not have a nidus⁷.

There are several diagnostic modalities available, including angiography, magnetic resonance imaging, and color Doppler ultrasound. For suspected AVM, Doppler ultrasonography and MRI are the modalities of choice, as they not only define a uterine AVM accurately, but

may also non-invasively assess the degree of pelvic involvement. Ultrasonographic gray scale findings of uterine AVMs are usually subtle and nonspecific, showing slight myometrial heterogeneity and small anechoic spaces in the myometrium⁴. Diagnosis of a uterine AVM cannot be made on gray scale sonography alone; a supplementary Doppler study would have to be done, on which characteristic findings would be a tangle of vessels with multidirectional, low-resistance, high-velocity flow producing a “color mosaic” pattern⁴. Doppler studies were implemented to correctly diagnose 2 of our cases presented, with the arteriovenous shunting and color mosaic pattern identified. Three-dimensional Doppler sonography also establishes additional evaluation by showing a clearer view of the orientation of its tortuous vessels. It is also used to monitor AVMs for response to treatment or recurrence after embolization⁹. Even with the use of gray scale and color doppler, there may still be some overlap with other pregnancy related diagnoses, and it is important to take serum β -hCG levels into account. β -hCG would be expectedly be grossly elevated in gestational trophoblastic diseases and weakly elevated in retained products of conception.

Angiography, however, still remains the gold standard for diagnosis. It would be based on the appearance of uterine arteries feeding a tortuous hypertrophic arterial mass, with large accessory feeding vessels, and early drainage via enlarged veins⁴. It is not used commonly for diagnostic purposes alone, but only when therapeutic embolization is considered.

Treatment of symptomatic uterine AVM is based on the location, the extent, and the desire for future fertility, and clinical status of the patient. Traditionally, hysterectomy and removal of the AVM has been the way of treatment of such disorders. However, an effective alternative is embolization of the uterine artery, which is less invasive and has the benefit of fertility preservation. Patients presenting with a single episode of bleeding and who are hemodynamically stable may be treated more conservatively, but if anemic or hemodynamically unstable, should be referred for angiography and embolization. Recurrent bleeding also necessitates embolization but does not correlate with the size of an AVM on imaging, but rather on the patient's clinical status⁴.

Many patients will remain asymptomatic, suggesting that traumatic AVMs do spontaneously regress⁴. In cases of recurrence, surgical treatment should be considered. Selective ligation of the vessels supplying the malformation is an effective treatment option when conservative methods have failed and uterine preservation is of primary concern. In cases of postmenopausal women or those not desirous of pregnancy,

hysterectomy remains the treatment of choice. It is also indicated as an emergency treatment in case of life-threatening or refractory hemorrhage, as seen in the first case presented.

In the cases presented, although desire for future fertility was taken into account, a hysterectomy was performed on case 2 due to the financial burden of performing a more complicated procedure. However, all other cases presented opted to preserve fertility and underwent Bilateral hypogastric artery ligation followed by excision of the endometrial mass and right uterine artery embolization with gel foam respectively.

Following embolization, occurrences of pregnancy are rare, although not impossible. Spontaneous abortion and growth retardation have been attributed to poor vascularization of the treated areas interfering with placental development and maternal-fetal perfusion. Hyperselective embolization to obstruct the affected vessels while preserving the other arterial vessels appears to improve the obstetric outlook¹⁰.

SUMMARY

In summary, we presented 4 cases of uterine arteriovenous malformation, all presenting with heavy, refractory bleeding. These cases were diagnosed using gray scale and color Doppler studies, as well as CT angiography. Treatment differed based on specific clinical findings, patient status, and desire for fertility preservation. And although more advanced interventions have been discovered, surgical management like a hysterectomy may still be performed when other options are unavailable or not feasible. Diagnostic modalities and treatments employed should be individualized to every patient's needs.

In a patient presenting with unexplained, intermittent vaginal bleeding, especially with a history of previous operations, or curettages, it is worth considering uterine arteriovenous malformation as a probable cause. The lack of any hard set rules or algorithms, as well as the scarcity of information regarding and dealing with this condition, emphasizes the importance of documentation and dissemination of literature. A high index of suspicion is necessary to properly work up and identify or exclude this diagnosis. ■

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